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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/661,588	09/15/2003	Sven Schreder	MERCK-2168D1	8058

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EXAMINER	
SPIVACK, PHYLLIS G	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
08/18/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@mwzb.com

Office Action Summary	Application No.	Applicant(s)	
	10/661,588	SCHREDER ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5 and 9-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-5, 9-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Upon reconsideration, a previous indication of allowability is withdrawn.

Applicants' Response filed May 12, 2009 is acknowledged. Claims 1, 3-5 and 9-16 remain under consideration.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The abstract of the disclosure is objected to because processes for the production of pharmaceutical preparations are not claimed in the present application. Correction is required. See MPEP § 608.01(b).

Claims 1, 3-5 and 9-16 were rejected under 35 U.S.C. 103(a) as being unpatentable over Reynolds et al., U.S. Patent 3, 808,332, in view of Lindenbaum E., WO 93/04691, and further in view of Jacobs et al., US 2005/0003491, in the last Office Action. It was asserted Reynolds teaches a combination of L-thyroxine and L-triiodothyronine that are physically admixed. Therefore, no organic solvent is present. See column 7, lines 65-67. See Composition I, column 7, where cornstarch is employed as a filler, and Composition J, where lactose and microcrystalline cellulose are employed as fillers. As required by instant claim 3, Reynolds teaches a concentration range of l-thyroxine of 100-300 mcg. Fillers such as lactose, maize starch and microcrystalline cellulose are conventional excipients. Reynolds fails to include gelatin in the combination. However, Lindenbaum teaches pharmaceutical preparations comprising levothyroxine or triiodothyronine and gelatin that are manufactured in solid forms, such as creams or powders, without organic

solvents. See claims 13 and 19, as well as page 17, lines 16-18. A micronized form of levothyroxine with a particle size between 5 and 25 μm is conventional.

Jacobs teaches the inclusion of gelatin in solid pharmaceutical formulations comprising proteins, such as tablets. See page 174, paragraph 4072.

Applicants argue one skilled in the art would not look to the topical formulation disclosure of Lindenbaum for any suggestion of the use of gelatin. Applicants urge neither Reynolds nor Lindenbaum suggests formulations using gelatin as a binder in a tablet or solid formulation. Regarding Jacobs, Applicants agree the disclosed compositions may be in the form of a tablet or capsule and may additionally contain a solid carrier as gelatin. Applicants argue a skilled worker dealing with the problem of stabilization of levothyroxine would not look towards a broad generic disclosure that deals with numerous administration forms of different proteins.

Applicants' arguments are not persuasive. Gelatin is conventionally employed as a binder in tablet formulations because of its well-established cohesive qualities. One skilled in the art of formulation chemistry would have been motivated to prepare pharmaceutical formulations comprising L-thyroxine and, optionally, triiodothyronine, utilizing gelatin, in a solid form without organic solvents.

The showing presented in the Declaration filed February 13, 2008 under 37 CFR 1.132, is not commensurate in scope with the present claims. While Formulations B and C were demonstrated to have increased stability of

levothyroxine, said formulations are drawn to specific ratios and amounts of active agent and excipients, whereas the instant claims are in no way limited to any particular amounts of active compound and gelatin. Further, in Formulation A, it is unclear whether or not hydroxypropyl methylcellulose (HPMC) imparts an unexpected *destabilizing* effect on levothyroxine sodium. If such were the case, it would not be gelatin providing an unexpected stabilizing effect, but rather HPMC providing an unexpected destabilizing effect. As such, in the absence of a showing that the alleged stabilizing effect of gelatin occurs over a broad range of amounts and ratios of active agent and gelatin in the claimed tablets, the Examiner is not persuaded that Applicants have demonstrated an unexpected result commensurate in scope with the claims. Furthermore, Applicants have only provided a comparison of HPMC and gelatin as binders. It cannot therefore be said that gelatin provides an unexpected stabilizing effect without showing comparisons to other known pharmaceutical binders.

No claim is allowed. However, favorable consideration would be given to claims drawn to the formulations disclosed in Examples 1-3 on pages 5-7 of the specification.

THIS ACTION IS MADE FINAL. Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this Final Action is set to expire THREE MONTHS from the mailing date of this Action. In the event a first reply is filed within TWO MONTHS of the mailing date of this Final Action and the Advisory Action is not mailed until after the end of the THREE-MONTH shortened

statutory period, then the shortened statutory period will expire on the date the Advisory Action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the Advisory Action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this Final Action.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached from 10:30 to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel, can be reached 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

August 12, 2009

/Phyllis G. Spivack/
Primary Examiner, Art Unit 1614